# Modeling fluid flow in developing embryonic vertebrate hearts

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***Abstract* - The embryonic vertebrate heart starts pumping long before the formation of valves and chambers. Although all our lives rely on this early pumping mechanism, little is still known about the driving forces behind cardiac development. To validate the hypothesis that the morphogenesis of the heart is guided by blood flow patterns, one makes use of optically transparent zebrafish embryos which are morphologically comparable to human embryonic hearts in early stage.**

**To determine the flow patterns we plan to build an upscaled model of a peristaltically pumping embryonic heart based on *in vivo* microscopic images. We will use experimental (particle image velocimetry) and numerical (computational fluid dynamics) techniques to estimate local blood velocities within the embryonic heart and validate the results with *in vivo* physiological data. Doing so for different stages in heart development will likely provide insight in the underlying driving biomechanical forces.**

***Keywords* - Embryonic heart, blood flow, peristaltic, CFD, PIV**

## I. Introduction

In the human embryo, the heart begins to pump blood about three weeks post conception. In this stage the heart has neither chambers nor valves but only consists of a contractile tube.

The subsequent morphological development of an embryonic heart is dependant of a balanced interaction between a genetic program, fluid mechanical stimuli and the inter- and intracellular processes that link them [1]. While the genetics are intensely studied, the analysis of the influence of blood flow patterns and biomechanical forces has advanced more slowly due to the difficulties in mapping intracardiac flow *in vivo*. Numerous *in vitro* studies reveal that epithelial heart cells are sensitive to mechanical stimuli such as wall shear stress and changes in pressure caused by a pulsatile blood flow.

To map the intracardiac flow we are forced to use optical techniques as the spatial and temporal resolution of most X-ray based visualization techniques is limited. The optical accessibility, the numerous genetic studies and the comparability with human morphological heart development makes the zebrafish (*Danio rerio*) an ideal model to analyze the impact of the blood on the cardiogenesis of the vertebrate heart.

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## II. Materials and Methods

### *A. In vivo mapping of the flow in a zebrafish embryonic heart*

Thanks to the collaboration with the Institute of Human Genetics International Centre for Life (Newcastle upon Tyne, UK) we have access to high speed confocal images of 20 complete heart cycles of a 30 hours post fertilization zebrafish embryo. This early stage, prior to valve formation, shows already a pumping heart tube. The images were taken at 207 frames per second and magnified by 40 times allowing us to track individual blood cells (Figure 1).

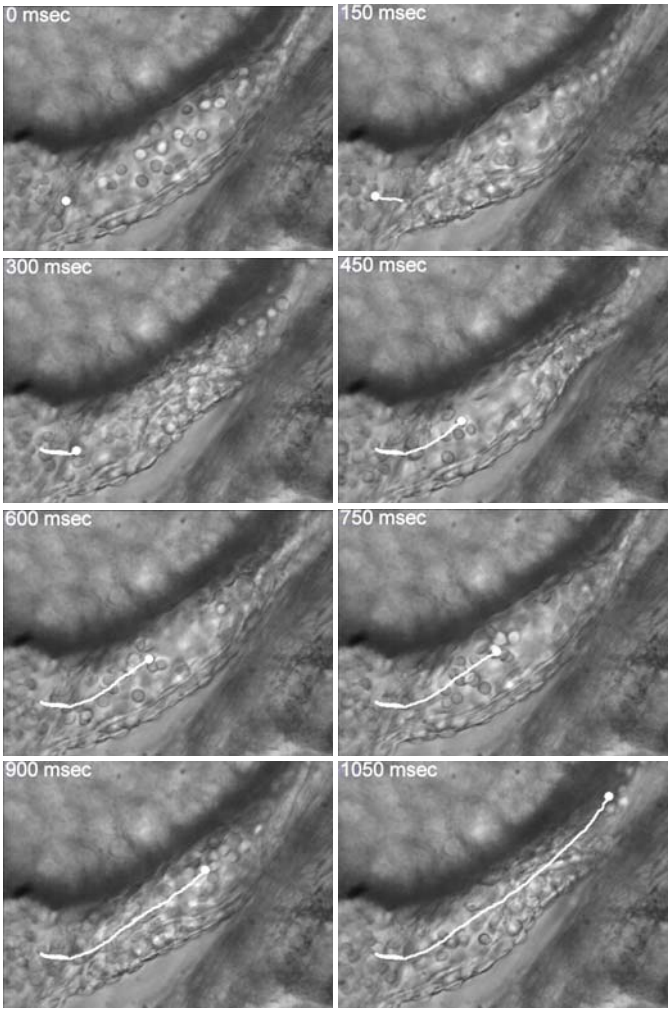


Figure 1. Image sequence showing a track of one blood cell of an embryonic zebrafish heart 30 hours post fertilization starting from the end of the diastole.

A first attempt to derive the blood flow pattern involves manual tracking of the individual blood cells. As the spatial and the temporal resolution are known we are able to calculate velocities and accelerations (Figure 2). Averaging over a sufficiently high number of heart cycles will provide insight in flow patterns.

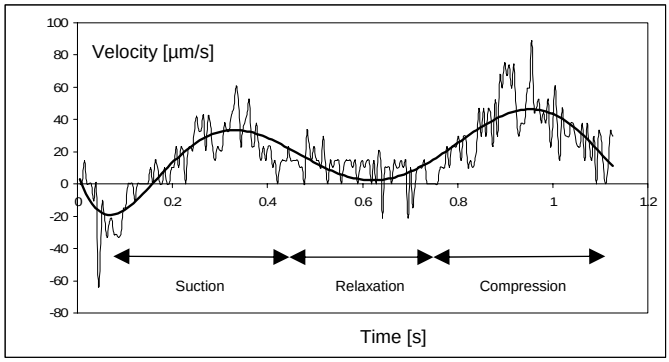


Figure 2. Graph showing the velocity over time of the blood cell shown in the image sequence of Figure 1. Qualitatively a suction, a relaxation and a compression phase of the heart tube is defined keeping in mind that suction and compression is dependent of the position of the blood cell compared to the site of the contraction.

### *B. Modeling the pumping mechanism*

As the intracardiac flow is caused by the contractions of the heart tube it is important to understand the pumping mechanism in order to link this to the morphogenesis of the heart. As the pumping mechanism changes during the formation of valves the flow pattern will likely change, giving other mechanical stimuli to the epithelial wall cells [2].

It has long been suggested that the heart functions initially as a peristaltic pump with a wave propagating from the venous to the arterial end of the heart tube. Recent research, however, led to the hypothesis of a dynamic suction pumping mechanism [3].

To evaluate the pumping mechanism we plan to build an upscaled hydraulic model of a peristaltically pumping heart (Figure 3).

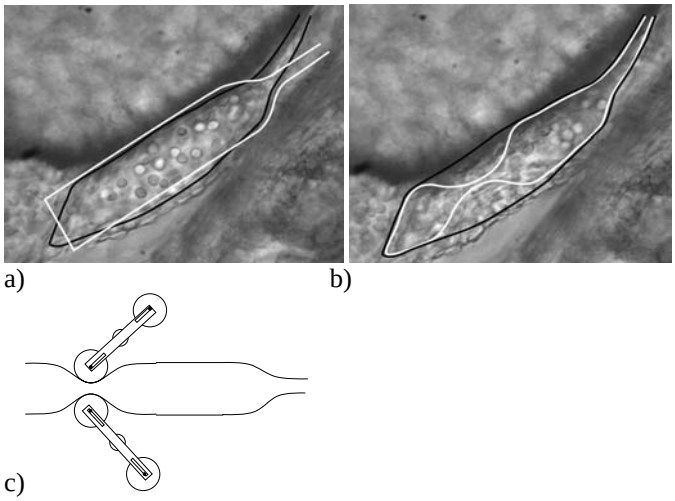


Figure 3. a) embryonic zebrafish heart at the end of the diastole (the wall is colored black and the idealized model is colored white); b) heart in systole, wall colored white (compared to the heart at the end of the diastole colored black); c) schematic view of an upscaled hydraulic model of the embryonic heart derived from the idealized model in a).

2D Particle image velocimetry will provide a quantitative representation of the flow field in time. Comparison with the averaged results of the blood cell tracks will give exclusion about the initial embryonic heart pumping mechanism being peristaltic or not.

### *C. Numerical modeling of flow field and estimation of wall shear stresses*

Estimating wall shear stresses caused by the fluid flow is crucial as the morphogenesis of the embryonic heart is believed to be influenced by mechanical stimuli. Normally these shear stresses are derived from the spatial gradient of the velocity, but with a relative blood cell diameter of 1/5 compared to the heart tube diameter the spatial resolution will be too coarse.

Therefore we choose to model the fluid flow with a Computational Fluid Dynamics (CFD) code. As the high speed confocal images were taken at cellular level it is possible to track the motion of epithelial cells of the heart wall. Imposing the exact same wall movement as a boundary condition in the CFD code, it is possible to derive the local fluid velocity. The boundary conditions at the in- and outlet can be estimated by comparing the computed results with the averaged blood cell velocities. Once a validated solution of the fluid flow is obtained we can estimate the shear stresses on the heart tube wall.

## III. CONCLUSIONS

Understanding the fluid dynamics of the intracardiac blood flow is necessary in order to obtain a better insight in the morphogenesis of the embryonic vertebrate heart. With the aid of experimental and numerical techniques it is possible to obtain a quantitative comparison over different heart development stages and to link the influence of mechanical stimuli to morphological changes.

## ACKNOWLEDGEMENTS

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